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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,694	12/21/2004	Michael Chopp	1059.00106	2465

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EXAMINER	
WEBB, WALTER E	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
09/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,694	CHOPP, MICHAEL	
	Examiner	Art Unit	
	WALTER E. WEBB	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 8-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 8-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 6/26/2009, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112--previous

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 8-13 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administering sildenafil or hMCS to ischemic rats, does not reasonably provide enablement for promoting neurogenesis in an ischemic patient in general by administering a phosphodiesterase type 5 inhibitor and cellular therapy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

A declaration by Dr. Micheal Chopp was submitted on 6/26/2009 to rebut this rejection. The affiant argues that the mechanism of action of neurogenesis in the rat is also present in human studies. Affiant cites PNAS August 29, 2006 and Nature Medicine 2002 for support. However, it is not clear, and affiant does not point this out, how the cited references support this argument. The PNAS article of August 29, 2006

distinguishes the rodent model of stroke from human in regard to source of new neurons stating, "In rodent models of stroke, the source of new neurons that migrate to ischemic brain areas appears to be the subventricular zone (6-9). In human biopsy specimens, the source of these cells in unclear . . . ." (See pg. 13201, left column, 2nd paragraph.) The Nature Medicine article of 2002 only discussed results obtained from a rat model (see Methods at pg. 969) and made no comparison to human data. Neither reference teaches that the mechanism of action of neurogenesis in the rat is also present in human studies.

Affiant argues that the statement cited in Bjorklund et al., in regard to the need for better knowledge of biological mechanisms of improvement for use of cellular therapy for humans, was "someone's OPINION, published 9 years ago, with no basis in fact. Affiant further argues that the authors of the reference are not stroke experts, and are not discussing cell or pharmacological therapies that stimulate production of the brain's stem cells. However, it is not clear how the statement of Bjorklund et al. is an opinion with no basis in fact, when the reference relied on studies involving rats showing success after stroke treatment but only under certain conditions e.g. type of cells used, type of injury, environment after administering therapy (see pg. 541). It is unclear how the reference cannot be relied on for what it teaches even if it is true, and affiant does not show proof of this, that the authors are not stroke experts. Furthermore, applicant's invention is not drawn to stimulation of the production of the **brain's stem cells**. The Bjorklund et al. reference is a proper reference since it discusses administration of cellular therapy to a patient as per the instant claims.

Affiant argues that the comments of Johansson, which raised doubt as to the regeneration of central axons in higher mammals, a merely comments that do not in anyway preclude Applicant's ability to stimulate recovery of function using cells of drugs. However, the reference was used to provide evidence that more guidance is needed in regard to promoting neurogenesis in humans. The references of Johansson and Bjorklund acknowledge successful treatment in rats but doubt the same success can be had in humans. They both caution that more guidance is needed to reasonably predict the same success in humans. The instant disclosure provides what is known in the art in regard to using cellular therapy in a rat model, but does description of how the same success can be had in humans. Thus the disclosure does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103--previous

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 8, 10 and 12 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Black (US 6,043,223) in view of Yoshimura et al., (PNAS 2001).

Applicant argues that there is no scientific of logical connection between the present invention and the Black patent. However, like the patent to Black, applicant claims a administering a phosphodiesterase type V inhibitor to an ischemic patient.

Applicant also argues that the promotion of neurogenesis by the methods of Black is a logical flaw. However, in the declaration discussed above, the affiant states that "the group of phosphodiesterase type 5 inhibitors encompasses a well defined group, and one skilled in the art would expect one PDE5 inhibitor would function in the same manner as another." Thus, it is logical to expect that administration of zaprinast to an ischemic patient in need of neurogenesis promotion would promote neurogenesis. Furthermore, it is noted that the instant claims do not recite a specific PDE5 inhibitor.

2) Claims 2, 9, 11 and 13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Black (supra) as applied to claim1, 8, 10 and 12 above, and further in view of Labat (Biomed Pharmacotherapy 2001).

Labat teaches the use of mesenchymal stem cells as cellular therapy (see pg. 181, left col., 4th paragraph).

Applicant argues that Labat does not teach that adult stem cells can stimulate recovery of function and amplify the endogenous production of **brain stem cells** that contribute to recovery of function. However, this is not a limitation of the instant claims and therefore need not be taught in Labat.

Applicant argues unexpected synergistic results with respect to the combination of PDE5 inhibitor and cellular therapy of MSCs. However, unexpected results must be

established by factual evidence. Due to the absence of tests combining a PDE5 inhibitor and cellular therapy of MSCs to promote neurogenesis, applicant's assertions of unexpected results constitute mere argument.

Nonstatutory Obvious-type Double Patenting--Previous

1) Claims 1, 8, 10, 12 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6-8, and 14-17 of copending Application No. 10/075,715.

2) Claims 1, 8, 10, 12 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6 and 7 of copending Application No. 10/018,201.

In regard to these rejections applicant states that a terminal disclaimer can be provided upon the indication of allowance of the pending claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 8:00am-4:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Walter E. Webb
/Walter E Webb/
Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612